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Effect of Age on Left Ventricular Function During Exercise in Patients With Coronary Artery Disease

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The purpose of this study was to assess the effect of age on left ventricular performance during exercise in 79 patients with coronary artery disease (≥ 50% narrowing of one or more major coronary arteries). Fifty patients under the age of 60 years (group I) and 29 patients 60 years or older (group II) were studied. Radionuclide angiograms were obtained at rest and during symptom-limited upright bicycle exercise. The history of hypertension, angina or Q wave myocardial infarction was similar in both groups. Multivessel coronary artery disease was present in 30 patients (60%) in group I and in 19 patients (66%) in group II (p = not significant).

There were no significant differences between the two groups in the hemodynamic variables (at rest or during exercise) of left ventricular ejection fraction, end-diastolic volume, end-systolic volume and cardiac index. Exercise tolerance was higher in group I than in group II (7.8 ± 0.4 versus 5.7 ± 0.4 minutes, p = 0.009), although the exercise heart rate and rate-pressure product were not significantly different between the groups. There was poor correlation between age and ejection fraction, end-diastolic volume and end-systolic volume at rest and during exercise. Abnormal left ventricular function at rest or an abnormal response to exercise was noted in 42 patients (84%) in group I and in 25 patients (86%) in group II (p = not significant).

Thus, in patients with coronary artery disease, age does not influence left ventricular function at rest or response to exercise. Older patients with coronary artery disease show changes in left ventricular function similar to those in younger patients with corresponding severity of coronary artery disease.

The cardiovascular system is one of many systems influenced by the aging process. Although a decrease in work performance with advancing age has been recognized for many years (1), the effect of age on cardiovascular hemodynamics during exercise has only recently been addressed (2–7). Research on aging is plagued by the problem of separating disease-related changes from age-related changes in cardiac function, particularly because there is a high incidence of ischemic heart disease in elderly people (8–10). Recently, noninvasive assessment of left ventricular performance at rest and during exercise by means of radionuclide angiography has been made possible without the need for cardiac catheterization (11–16).

Port et al. (17) demonstrated the effect of aging on left ventricular performance during exercise in healthy volunteers. They attributed the abnormal response in left ventricular ejection fraction to exercise in patients over the age of 60 to the normal aging process. Because these data have an important effect on decision making in elderly patients with suspected coronary artery disease, we undertook this study to assess the effect of age on left ventricular function at rest and during exercise in patients with coronary artery disease documented by coronary arteriography.

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Methods

Patients. We reviewed our records and identified 79 consecutively studied patients with coronary artery disease documented by coronary arteriography, who had had rest and exercise radionuclide ventriculography within 8 weeks before cardiac catheterization (80% of the patients) or after catheterization (the remaining 20% of the patients). Each patient had at least 50% diameter narrowing of one or more major coronary arteries. None of the patients had had coronary artery bypass surgery, and none had concomitant valvular heart disease.

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Exercise testing. A detailed history and complete physical examination were obtained for each patient before exercise testing. Patients were exercised at least 2 hours after a light meal. Cardiac medications were not routinely discontinued before exercise. Patients were familiarized with the exercise protocol. Twelve lead electrocardiograms were obtained before exercise (with patients in the supine and standing positions and during hyperventilation), at peak exercise and at the conclusion of the test. Two electrocardiographic leads were monitored constantly, and blood pressure was measured by the cuff method every 2 minutes during exercise and recovery. Symptom-limited multistage exercise testing was performed with the patient in the upright position on an electronically braked bicycle ergometer, starting at a work load of 200 kilopond-meters (kpm)/min and increasing by 100 kpm/min every 2 minutes until the exercise end point was reached. The end points of exercise were defined as severe angina pectoris with or without ST segment depression, excessive fatigue, weakness or shortness of breath, hypotension, dizziness and frequent complex arrhythmias.

Exercise electrocardiographic interpretation. The exercise electrocardiograms were interpreted as positive, negative or inconclusive. A positive exercise electrocardiogram was indicated by: 1) 1 mm or more horizontal or downsloping ST segment depression; 2) slowly rising ST segment with at least 1.5 mm depression 0.08 second after the J point; or 3) in the presence of ST segment depression at rest, 2 mm more of ST segment depression 0.8 second after the J point. An exercise electrocardiogram was considered negative when the patient achieved at least 85% of the maximal predicted heart rate in the absence of ST segment changes. The exercise electrocardiogram was considered inconclusive or uninterpretable when: 1) the patient failed to achieve at least 85% of the predicted maximal heart rate in the absence of ischemic ST segment changes; 2) ST segment depression (≥ 0.5 mm) was present in the elec-

Table 1. Clinical, Hemodynamic and Coronary Arteriographic Data According to Age in Patients With Coronary Artery Disease

	Group I (age < 60, n = 50)		Group II (age ≥ 60, n = 29)		
	no. (%)	Mean ± SEM	no. (%)	Mean ± SEM	p Value
Age (yr)		48 ± 1		65 ± 1	0.0001
Female/male ratio	3/47		6/23		NS
History of hypertension	19(38)		15(52)		NS
History of MI	33(66)		15(52)		NS
Propranolol therapy	34(68)		17(59)		NS
Q wave MI	17(34)		4(14)		NS
Rest HR (beats/min)		68 ± 2		68 ± 2	NS
Ex HR (beats/min)		118 ± 3		110 ± 3	NS
% Max pred		69 ± 2		71 ± 2	NS
Rest SBP (mm Hg)		124 ± 2		129 ± 4	NS
Ex SBP (mm Hg)		163 ± 4		161 ± 5	NS
Ex rate-pressure product (mm Hg·min^{1} × 10^{-3})		19.4 ± 2.3		17.7 ± 0.8	NS
Ex duration (min)		7.8 ± 0.4		5.7 ± 0.4	< 0.0009
Positive Ex ECG	22(44)		10(34)		NS
Ex angina	24(48)		8(28)		NS
Rest EF (%)		50 ± 2		52 ± 3	NS
Ex EF (%)		49 ± 2		51 ± 2	NS
Rest EDV (ml)		175 ± 6		173 ± 9	NS
Ex EDV (ml)		206 ± 7		191 ± 8	NS
Rest ESV (ml)		91 ± 7		88 ± 10	NS
Ex ESV (ml)		111 ± 8		97 ± 9	NS
Rest CI (liters/min per m^2)		2.8 ± 0.1		3.0 ± 0.2	NS
Ex CI (liters/min per m^2)		5.6 ± 0.2		5.3 ± 0.2	NS
Rest SBP/ESV (mm Hg·ml^{-1})		1.7 ± 0.1		2.0 ± 0.2	NS
Ex SBP/ESV (mm Hg·ml^{-1})		2.0 ± 0.2		2.1 ± 0.2	NS
CAD					
1 vessel	20(40)		10(34)		NS
2 vessel	21(42)		9(32)		NS
3 vessel	9(18)		10(34)		NS
CAD score		34 ± 6		35 ± 5	NS

CAD = coronary artery disease; CI = cardiac index; ECG = electrocardiogram, EDV = end-diastolic volume; EF = ejection fraction; ESV = end-systolic volume; Ex = exercise; HR = heart rate; max pred = maximal predicted; MI = myocardial infarction; NS = not significant; p = probability; SBP = systolic blood pressure; SBP/ESV = systolic blood pressure to end-systolic volume ratio; SEM = standard error of the mean.

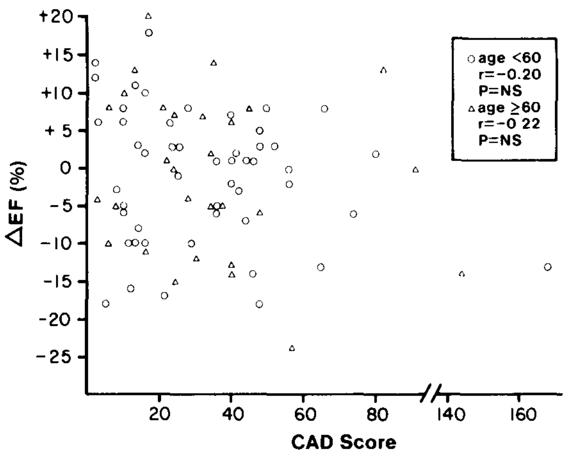


Figure 1. Correlation between coronary artery disease (CAD) score and change in ejection fraction (ΔEF) from rest to exercise. **Circles** represent patients in group I and **triangles** represent patients in group II.

trocardiogram at rest without 2 mm more of ST segment depression during exercise; or 3) bundle branch block, left ventricular hypertrophy or severe arrhythmias were present during the test. Exercise electrocardiograms were evaluated by qualified independent observers without knowledge of the results of the other tests.

Radionuclide angiography. Radionuclide angiography was performed by the first pass method with a computerized multicrystal gamma camera (Baird-Atomic Systems-77) equipped with a 1 inch (2.54 cm) parallel hole collimator positioned anterior to the precordium. A 20 gauge polyethylene catheter was inserted into a large basilic or jugular vein, and a 15 mCi bolus of technetium-99m pertechnetate dissolved in a volume of less than 1 cc was rapidly administered intravenously and flushed with 20 cc of normal saline solution. Precordial counts were recorded on frame intervals of 50 ms for the rest study and 25 ms for the exercise studies during the initial pass of the radionuclide through the central circulation. Background counts of the precordium were obtained for approximately 15 seconds. The second 15 mCi bolus of technetium-99m pertechnetate was injected at peak exercise while the patient continued to exercise; the subject's chest was stabilized against the collimator during injection to prevent excessive motion.

The radionuclide angiograms were analyzed with computer software incorporated into the multicrystal camera. We determined left ventricular ejection fraction and volumes using previously described methods (11–14).

Cardiac catheterization. Each patient underwent left and right heart catheterization, left ventriculography and coronary arteriography by standard techniques. Significant coronary artery disease was considered present if there was 50% or greater narrowing in the diameter of one or more of the major coronary arteries. The extent of coronary artery disease was quantified using the scoring system of Gensini (18). This system takes into consideration the location and severity of the stenoses in the major vessels and their branches, in addition to the effect of collateral vessels.

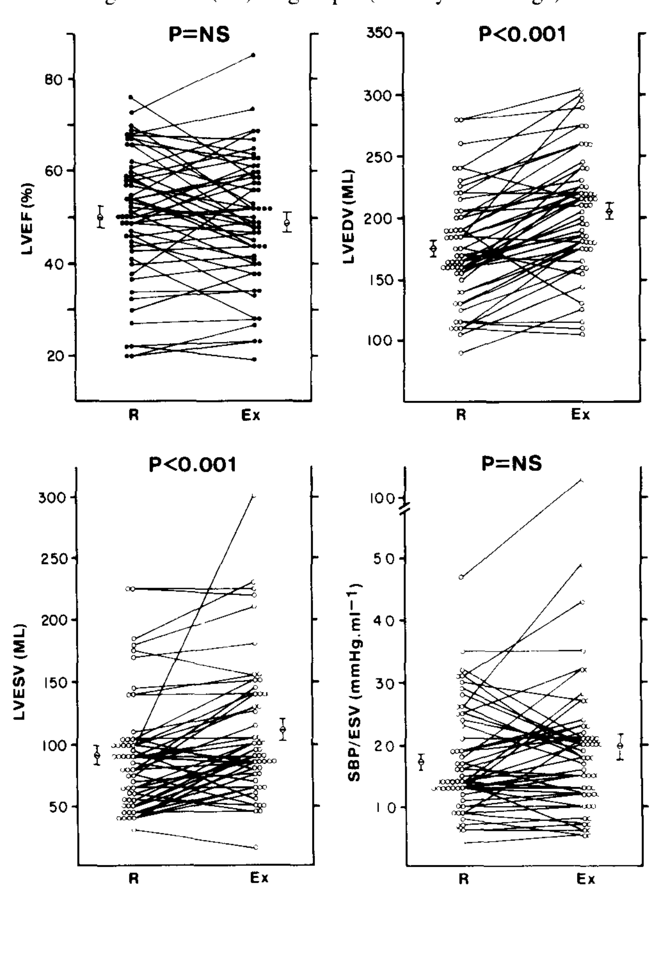
Statistical analysis. We determined the significance of the differences between groups using the analysis of variance or Fisher's exact test. The results were expressed as the mean ± standard error of the mean. A probability (p) value of less than 0.05 was considered significant. The relation between age and various independent variables was determined using a linear regression analysis.

Results

Patient characteristics. There were 9 women and 70 men with a mean age of 54 years (range 34 to 74). Thirty-four patients (43%) had a history of hypertension, 48 patients (61%) had a history of prior myocardial infarction and 21 patients (27%) had had a Q wave myocardial infarction. Thirty patients (38%) were in New York Heart Association functional class I, 36 patients (46%) were in class II and 13 patients (16%) were in class III.

Cardiac catheterization showed one vessel disease in 30

Figure 2. Left ventricular ejection fraction (LVEF), end-systolic volume (LVESV), end-diastolic volume (LVEDV) and systolic blood pressure to end-systolic volume ratio (SBP/ESV) at rest (R) and during exercise (Ex) in group I (< 60 years of age).



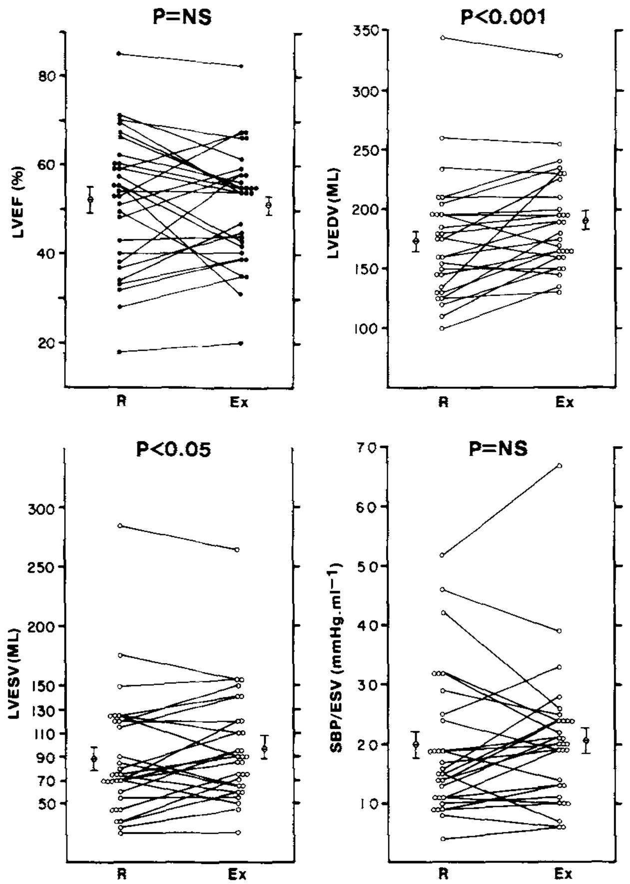


Figure 3. Left ventricular ejection fraction (LVEF), end-systolic volume (LVESV), end-diastolic volume (LVEDV) and systolic blood pressure to end-systolic volume ratio (SBP/ESV) at rest (R) and during exercise (Ex) in group II ($\geq$ 60 years of age).

patients (38%), two vessel disease in 30 patients (38%) and three vessel disease in 19 patients (24%). There were nine patients with left main coronary stenosis, eight of whom had other vessel involvement. Left main coronary stenosis was characterized as two vessel disease (left anterior descending and left circumflex arteries).

Age groups. There were 50 patients under the age of 60 years (group I) and 29 patients 60 years of age or older (group II) (Table 1). The age range in group II was 60 to 74 years (mean 65); 12 of the 29 patients were 65 years of age or older. There was no significant difference between the two groups in the incidence of Q wave myocardial infarction, propranolol therapy or the extent of coronary artery disease, as assessed by the number of diseased vessels and by the scoring system. Left main coronary stenosis was present in 5 patients (10%) of the 50 patients in group I and in 4 patients (14%) of the 29 patients in group II (p = not significant [NS]).

Age and left ventricular function. The correlation between the extent of coronary artery disease and ejection fraction in both age groups is shown in Figure 1. There were no significant differences in heart rate, blood pressure, left ventricular ejection fraction, end-diastolic volume, end-systolic volume, cardiac index or systolic pressure to end-systolic volume ratio in the two groups, either at rest or during exercise (Table 1, Fig. 2 and 3). The only difference between the two groups was in exercise duration; patients in group I ($<$ 60 years) exercised for 7.8 $\pm$ 0.4 minutes and patients in group II ($\geq$ 60 years) exercised for 5.7 $\pm$ 0.4 minutes ($p = 0.0009$). However, as already indicated, the exercise heart rate, systolic blood pressure and heart rate-blood pressure product were not different in the two groups. The results were unchanged when patients with Q wave infarction were excluded, with the exception of exercise heart rate and rate-pressure product (Table 2).

The ejection fraction at rest and its response to exercise, as well as the wall motion abnormalities at rest and during exercise are shown in Table 3. Fourteen (28%) of the 50 patients in group I had a normal ejection fraction response to exercise ($\geq$ 5% increase) compared with 11 (38%) of the 24 patients in group II (p = NS). An abnormal ejection fraction at rest ($<$ 50%), or abnormal ejection fraction response to exercise (a decrease or $<$ 5% increase) or wall motion abnormalities at rest or during exercise, or a combination of these, was present in 42 patients (84%) in group I and 25 patients (86%) in group II (p = NS).

There was no significant correlation between age and heart rate, systolic blood pressure, end-diastolic volume, end-systolic volume, cardiac index, ejection fraction or end-systolic pressure to end-systolic volume ratio, either at rest or during exercise (Table 4, Fig. 4). Finally, when the patients in group I were further subdivided according to their age ($<$ 50 and 50 to 59 years), the results were unchanged (Table 5).

Discussion

The effect of age on cardiovascular hemodynamics has been shown in normal subjects (3,6,17), but age-related changes in cardiovascular responses to exercise in patients with coronary artery disease are still not well understood. Although wall motion abnormalities and a decline in exercise ejection fraction during exercise have been reported with increasing frequency in patients without manifest coronary artery disease who are 50 years or older (17), it is not known whether these observations can be extended to patients with documented coronary artery disease (8). Accordingly, we used radionuclide angiography to evaluate the effect of age on left ventricular function at rest and during exercise in patients with coronary artery disease documented by coronary arteriography.

Effect of age on ventricular volume and ejection fraction during exercise. This study demonstrates that changes in left ventricular ejection fraction and volume during exercise are similar in older and younger patients. Abnormalities in left ventricular response to exercise are attributed

Table 2. Pertinent Data According to Age in the Absence of Q Wave Infarction

	Group I (age < 60, n = 33)	Group II (age ≥ 60, n = 25)	p Value
Age (yr)	48 ± 1	65 ± 1	< 0.0001
Rest HR (beats/min)	71 ± 2	69 ± 2	NS
Ex HR (beats/min)	122 ± 4	110 ± 3	< 0.03
Rest SBP (mm Hg)	126 ± 3	132 ± 4	NS
Ex SBP (mm Hg)	171 ± 4	165 ± 5	NS
Ex rate-pressure product (mm Hg·min^{-1} × 10^{-3})	20.9 ± 0.9	18.0 ± 0.8	< 0 03
Ex duration (min)	7.9 ± 0.5	5.6 ± 0.4	< 0.0009
Rest EF (%)	56 ± 2	54 ± 3	NS
Ex EF (%)	55 ± 2	53 ± 3	NS
Rest EDV (ml)	158 ± 6	168 ± 10	NS
Ex EDV(ml)	187 ± 7	186 ± 9	NS
Rest ESV (ml)	70 ± 5	83 ± 11	NS
Ex ESV (ml)	86 ± 6	91 ± 9	NS
Rest CI (liters/min per m^2)	3 1 ± 0.2	3.1 ± 0 2	NS
Ex CI (liters/min per m^2)	6.1 ± 0.3	5.3 ± 0.3	NS
Rest SBP/ESV (mm Hg·ml^{-1})	2 1 ± 0.2	2 2 ± 0.2	NS
Ex SBP/ESV (mm Hg·ml^{-1})	2.4 ± 0.3	2.2 ± 0.2	NS
CAD score	28 ± 4	29 ± 4	NS

Abbreviations as in Table 1.

to coronary artery disease rather than to the effect of age, because there was no difference between younger and older patients. Port et al. (17) studied 77 apparently healthy subjects and found abnormal ejection fraction responses to exercise and wall motion abnormalities that were age-related. Because cardiac catheterization was not performed, asymptomatic coronary artery disease could not have been ruled out in their patients. Austin et al. (19) recently demonstrated that age did not influence the specificity of rest and exercise radionuclide angiography in patients with normal coronary arteries.

It is evident from our study that changes in left ventricular function during exercise in older patients with coronary artery disease are not different from those in younger patients with similar extent of coronary disease. Our findings do not support the hypothesis that age has an added adverse effect on left ventricular function during exercise, apart from that due to coronary artery disease itself.

The changes in global left ventricular function during exercise should be interpreted in the context of preload, contractility, afterload and heart rate. The chronotropic response to exercise in patients with coronary artery disease is variable and influenced by age, medication, conditioning and the occurrence of myocardial ischemia during exercise. Older patients in our study achieved heart rates at peak exercise comparable with those of the younger patients. This finding denotes a higher (although insignificant) percent of maximal predicted heart rate in older patients, because the maximal predicated heart rate declines with age (2,20). In other words, exercise effort, as indicated by exercise heart rate achieved by older patients, was equal to or greater than

Table 3. Ejection Fraction (EF) and Wall Motion Abnormalities (WMA) in the Two Groups of Patients

	Group I (age < 60) No. (%)	Group II (age ≥ 60) No. (%)	p Value
Rest EF < 50%	21(42)	11(38)	NS
EF increase on Ex < 5%	36(72)	18(62)	NS
Rest WMA	15(30)	9(31)	NS
Ex WMA	22(44)	12(41)	NS
One or more of the above	42(84)	25(86)	NS

Abbreviations as before

Table 4. Correlation of Age With Hemodynamic Data During Exercise

	r Value	p Value
Ex HR (beats/min)	− 0.15	NS
Ex SBP (mm Hg)	− 0.04	NS
Rest EF (%)	− 0.04	NS
Ex EF (%)	− 0 05	NS
Δ EF from Rest to Ex	− 0.01	NS
Rest EDV (ml)	0.16	NS
Ex EDV (ml)	− 0.03	NS
Rest ESV (ml)	0 13	NS
Ex ESV (ml)	− 0.04	NS
Rest CI (liters/min per m^2)	0.13	NS
Ex CI (liters/min per m^2)	0.11	NS

r = correlation coefficient, other abbreviations as before.

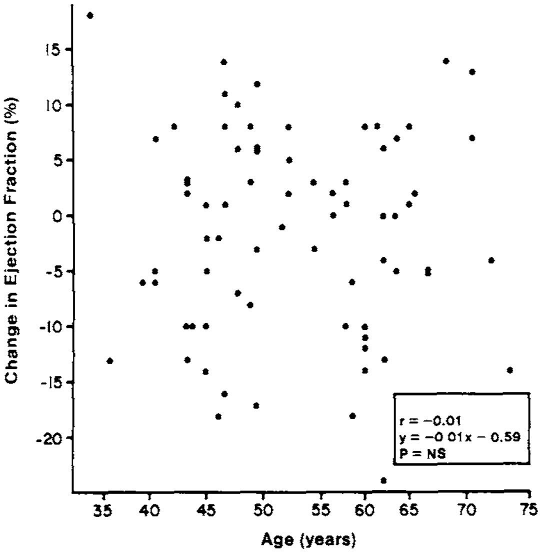


Figure 4. Lack of correlation between age and the change in left ventricular ejection fraction from rest to exercise.

that of younger patients, despite longer exercise duration in younger patients.

The effect of propranolol on left ventricular response to exercise has been investigated previously (21). Because in our study, a similar number of older and younger patients were administered beta-blocking agents, it is unlikely that propranolol or other beta-blocking agents affect age related changes in left ventricular function.

Older and younger patients did not differ in ejection fraction, end-diastolic volume (preload) and systolic blood pressure (afterload), either at rest or during exercise. Both groups had a slight but significant increase in end-diastolic volume from rest to exercise. These findings indicate that the Frank-Starling mechanism was responsible for augmenting performance during exercise in both groups of patients. This observation confirms an experimental study (22) demonstrating the absence of age difference in the active length-tension curve of the left ventricular trabeculae.

The fact that older patients had lower exercise capacity than younger patients (3,4,20) may be due to aging or to a deconditioning effect. Exercise conditioning, however, has not been shown to influence left ventricular ejection fraction response to exercise (23,24).

Role of extent of coronary artery disease. Because left ventricular function at rest and during exercise may be influenced by coronary artery disease, it is imperative to document the similarity in the extent of such disease in older and younger patients. In our study, the extent of coronary disease, as defined by the number of diseased vessels and by a scoring system, was similar in both groups. Moreover, manifestations of myocardial ischemia during exercise (angina or ST segment depression) were similar in both younger and older patients.

In conclusion, the response of left ventricular ejection fraction and volume to exercise in older patients is similar to that in younger patients who have comparable severity and extent of coronary artery disease. By itself, age does not have a significant effect on left ventricular function during exercise in patients with coronary artery disease.

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Table 5. Pertinent Data According to Age in Patients With Coronary Artery Disease

	Group I (age < 50, n = 31)	Group I (age 50 to 59, n = 14)	Group II (age ≥ 60, n = 29)	p Value
Rest HR (beats/min)	69 ± 2	68 ± 4	68 ± 2	NS
Ex HR (beats/min)	117 ± 3	121 ± 6	110 ± 3	NS
Rest SBP (mm Hg)	123 ± 3	125 ± 4	129 ± 4	NS
Ex SBP (mm Hg)	165 ± 6	160 ± 6	161 ± 5	NS
Ex rate-pressure product (mm Hg·min^{-1} × 10^{-3})	19.4 ± 0.9	19.5 ± 1.3	17 7 ± 0.8	NS
Ex duration (min)	7.7 ± 0.5	7.8 ± 0 6	5 7 ± 0.4	< 0.004
Rest EF (%)	50 ± 2	51 ± 4	52 ± 3	NS
Ex EF (%)	49 ± 2	50 ± 4	51 ± 2	NS
Rest EDV (ml)	172 ± 8	181 ± 11	173 ± 9	NS
Ex EDV (ml)	208 ± 9	201 ± 11	191 ± 8	NS
Rest ESV (ml)	88 ± 7	96 ± 13	88 ± 10	NS
Ex ESV (ml)	114 ± 10	106 ± 13	97 ± 9	NS
Rest CI (liters/min per m^2)	2.7 ± 0.1	2.9 ± 0.3	3.0 ± 0.2	NS
Ex CI (liters/min per m^2)	5.5 ± 0.2	5.8 ± 0.5	5 3 ± 0.2	NS
Rest Ex SBP/ESV (mm Hg·ml^{-1})	1.7 ± 0.1	1.9 ± 0.3	2.0 ± 0.2	NS
Ex SBP/ESV (mm Hg·ml^{-1})	1 8 ± 0 2	2.3 ± 0.5	2.1 ± 0.2	NS
CAD score	33 ± 6	34 ± 5	35 ± 5	NS

Abbreviations as before.

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